

## Gallic Acid and Cyclodextrins: Inclusion Complexes and Antimicrobial Activity

Eva Pinho<sup>1,2</sup>, Graça Soares<sup>2</sup>, Mariana Henriques<sup>1</sup>

<sup>1</sup>Institute of Biotechnology and Bioengineering, University of Minho, Campus Gualtar, Braga, Portugal,

<sup>2</sup>Department of Textile Engineering, University of Minho, Campus Azurém, Guimarães, Portugal

Gallic acid (GA), or 3,4,5-trihydroxybenzoic acid, is the commonest and simplest phenolic acid, with just one aromatic ring. This phenolic molecule has been described as antioxidant, anti-inflammatory and anti-tumour, also, antimicrobial and anti-fungal activity has been attributed to it. Besides all the GA biological activities, this compound is cheap, due to the easy plant extraction, and non-toxic. Thus, this phenolic acid has been widely used in food, drugs and cosmetic industry.

GA, as other phenolic compounds, is susceptible to environmental factors which may lead to the losing their structural integrity and bioactivity. This can be overcome by the encapsulation with cyclodextrins (CD). They are cyclic oligosaccharides arising from the degradation of starch; inexpensive and friendly to humans. CD are able to form an inclusion complex with a wide range of bioactive molecules, including hydrophobic ones, protect and modulate their release.

In the present work, the formation of an inclusion complex (IC) between  $\beta$ CD, HP $\beta$ CD (2-Hydroxypropyl- $\beta$ -cyclodextrin) or M $\beta$ CD (methyl- $\beta$ -cyclodextrin) and GA was analysed by UV spectrophotometry. The antimicrobial activity of the complexes was also assessed, by qualitative and quantitative methods. The influence of the buffer and pH on the formation of the IC and on the GA antimicrobial activity was also tested.

The IC formation was analysed in 2 buffer solutions ( $K_2HPO_4/KH_2PO_4$  and  $H_3PO_4/NaOH$ ). The GA and IC absorbance spectrum showed different appearances depending on the buffer used. When  $K_2HPO_4/KH_2PO_4$  was used, the IC spectrum presented some alterations on the  $\lambda_{max}$  comparatively to the GA spectrum. Since, the GA and ICs spectra obtained for the  $H_3PO_4/NaOH$  were similar, this buffer was selected.

The IC formation between GA and  $\beta$ CD, HP $\beta$ CD or M $\beta$ CD was analysed at pH 5, 7 and 8. Based on the results it was clear that the pH used affected the IC formation in the conditions tested. The  $\beta$ CD formed IC 1:1 with GA for all pH values, being the pH5 the most favourable. The same was observed for M $\beta$ CD, but these CD had the lowest values for the association constant, meaning that the IC formation between M $\beta$ CD and GA is not very efficient. Regarding the HP $\beta$ CD, in neutral pH the IC formed was 1:2 and for the others pH was 1:1, pH5 was the most favourable for the IC formation and pH7 the least.

The antimicrobial activity was assessed for the best combinations of GA/CD ( $\beta$ CD pH5 and pH7; HP $\beta$ CD pH5 and pH8). For all the IC tested, the antimicrobial activity of GA was improved or alike to the GA without encapsulation. To the authors knowledge, the IC formation between HP $\beta$ CD or M $\beta$ CD and GA has not been reported until now, as well as the antimicrobial activity of the IC  $\beta$ CD/GA and HP $\beta$ CD/GA.

**Keywords:** gallic acid; phenolic acid, encapsulation, cyclodextrin, inclusion complex, antimicrobial activity.